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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,337	01/28/2005	Kevin R. Lynch	00812-03	5792

34444 7590 06/14/2006

UNIVERSITY OF VIRGINIA PATENT FOUNDATION
250 WEST MAIN STREET, SUITE 300
CHARLOTTESVILLE, VA 22902

EXAMINER

FREISTEIN, ANDREW B

ART UNIT PAPER NUMBER

1626

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/523,337	Applicant(s) LYNCH ET AL.	
	Examiner Andrew B. Freistein	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-33 are currently pending in the instant application.

Priority

This application is a 371 of PCT/US03/23768, filed 07/30/2003, which claims benefit of US Provisional Application No. 60/399,545 filed on 07/30/2002 and US Provisional Application No. 60/425,595, filed 11/12/2002.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

Lack of Unity Requirement

Claims 1-31 are drawn to more than one inventive concept (as defined by PCT Rule 13), and accordingly, a restriction is required according to the provision of PCT Rule 13.2.

PCT Rule 13.2 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention).

PCT Rule 13.2 states unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.

Annex B, Part 1 (b), provides that "special technical features" mean those technical features, which, as a whole, define a contribution over the prior art.

Annex B, Part 1 (e), provides combinations of different categories of claims and states:

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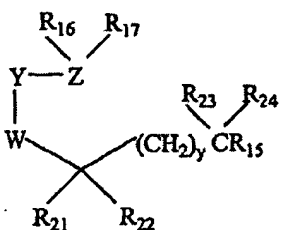
"The method for determining unity of invention under Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application:

- (i) in addition to an independent claim for a given product, an independent claims for a process specially adapted for the manufacture of the said product, and an independent claim for use of the said product, or
- (ii) in addition to an independent claim for a given process, an independent claim for an apparatus or means specially designed for carrying out the said process, or
- (iii) in addition to an independent claim for a given product, and independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for an apparatus or means specially designed for carrying out the said process,..."

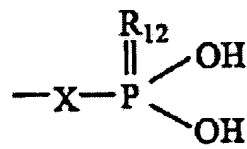
This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Due to numerous and widely divergent variables in the compound of Formula (I), for example: W, X, Y, Z, n, m, p, q, n, R², R³, R¹¹, R¹⁵, R¹⁶, R¹⁷, R²¹, R²², R²³, R²⁴, etc., a precise listing of inventive groups cannot be made. The following groups are exemplary:

Group I: Claims 1-23 (in part), drawn to products of the formula



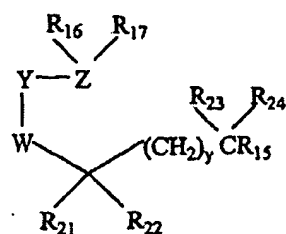
, wherein R₂₃ and R₂₄ are each H; R₁₅ is



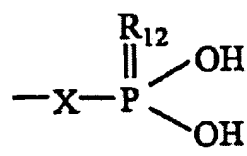
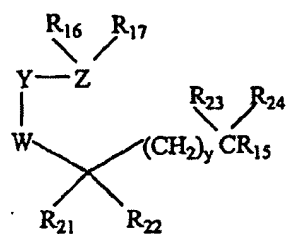
; R₁₂ is

O; X is O; y is 0; R₂₁ is NH₂; R₂₂ is H; W is (CH₂)_nNH(CO); n is 0; Y is a bond; Z is CH₂; R₁₆ is C₅-C₁₂alkyl; and R₁₇ is H.

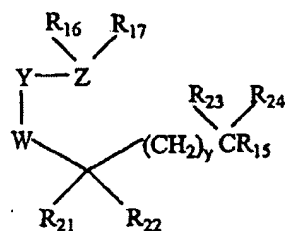
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Group II: Claims 1-23 (in part), drawn to products of the formula

, wherein R_{23} and R_{24} are each H; R_{15} is hydroxyl; y is 0; R_{21} is NH_2 ; R_{22} is H; W is $(\text{CH}_2)_n\text{NH}(\text{CO})$; n is 0; Y is a bond; Z is CH_2 ; R_{16} is $\text{C}_5\text{-C}_{12}\text{alkyl}$; and R_{17} is H.

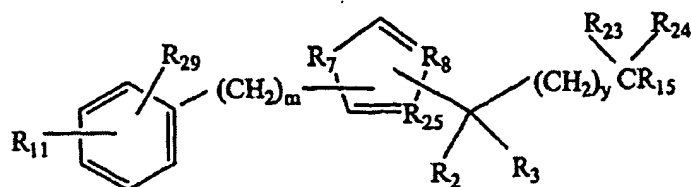
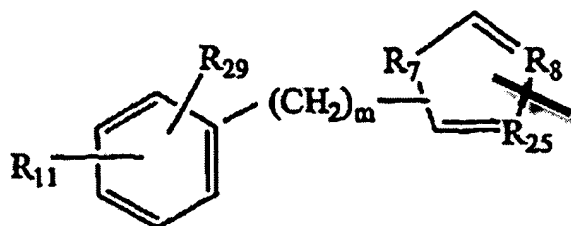
Group III: Claims 1-23 (in part), drawn to products of the formula

, wherein R_{23} and R_{24} are each H; R_{15} is O; X is O; y is 0; R_{21} is NH_2 ; R_{22} is H; W is $(\text{CH}_2)_n\text{NH}(\text{CO})$; n is 0; Y is a bond; Z is aryl; R_{16} is $\text{C}_5\text{-C}_{12}\text{alkyl}$; and R_{17} is H.

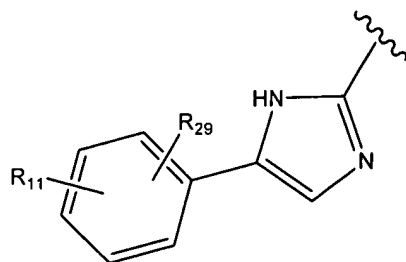
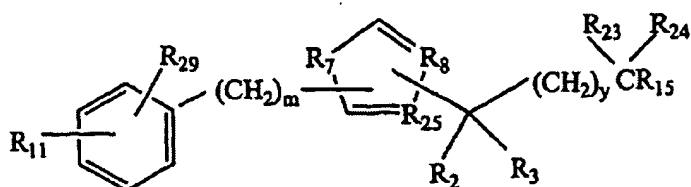
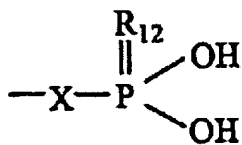
Group IV: Claims 1-23 (in part), drawn to products of the formula

, wherein R_{23} and R_{24} are each H; R_{15} is hydroxyl; y is 0; R_{21} is NH_2 ; R_{22} is H; W is $(\text{CH}_2)_n\text{NH}(\text{CO})$; n is 0; Y is a bond; Z is halo substituted aryl; R_{16} is $\text{C}_5\text{-C}_{12}\text{alkyl}$; and R_{17} is H.

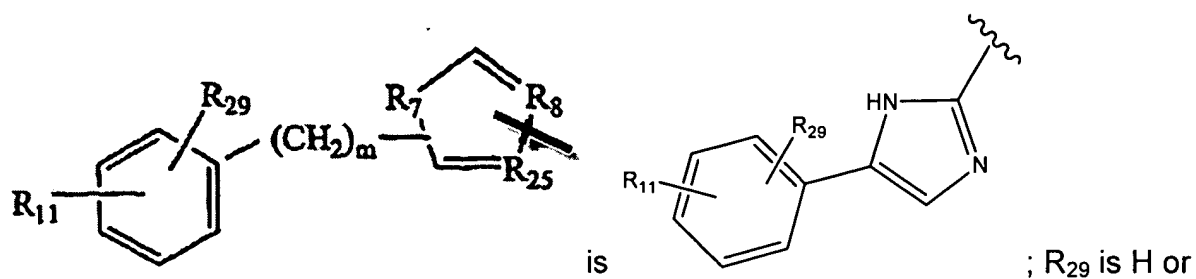
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Group V: Claims 1-23 (in part), drawn to products of the formula, wherein R_{23} and R_{24} are each H; R_{15} is hydroxyl; y is 0; R_2 is NH_2 ; R_3 is H;

is

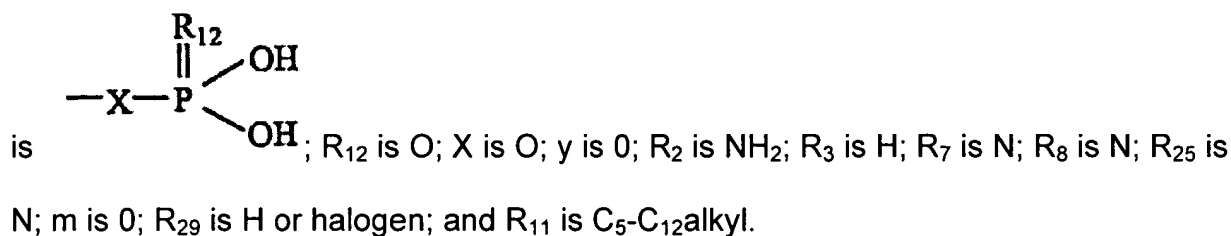
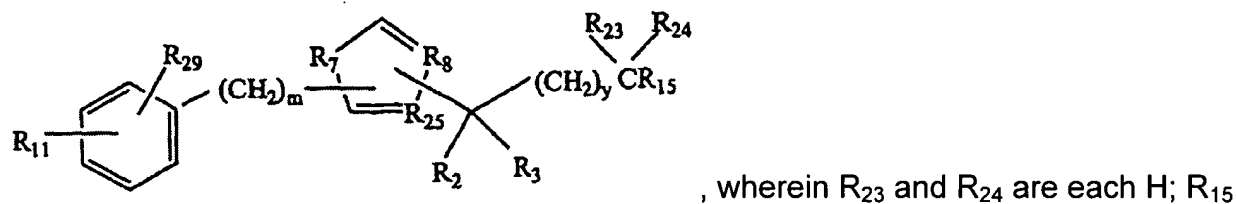
; R_{29} is H or halogen; and R_{11} is C_5 - C_{12} alkyl.**Group VI:** Claims 1-23 (in part), drawn to products of the formula, wherein R_{23} and R_{24} are each H; R_{15} is ; R_{12} is O; X is O; y is 0; R_2 is NH_2 ; R_3 is H;

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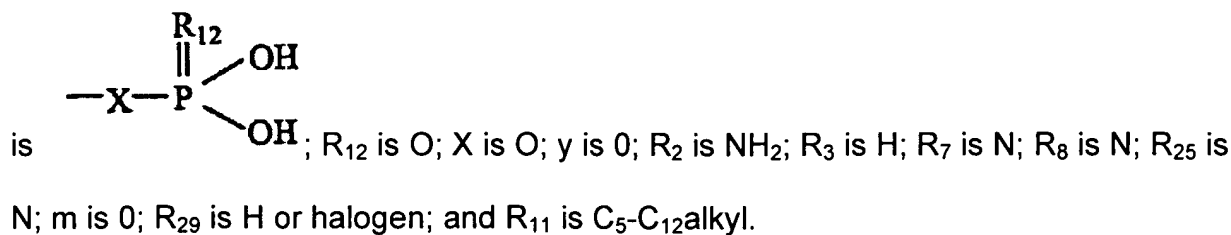
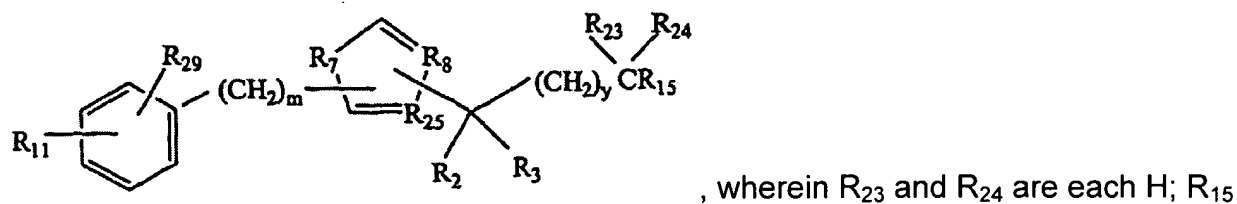


halogen; and R_{11} is C_5 - C_{12} alkyl.

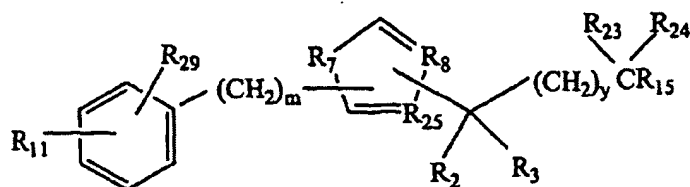
Group VII: Claims 1-23 (in part), drawn to products of the formula



Group VIII: Claims 1-23 (in part), drawn to products of the formula

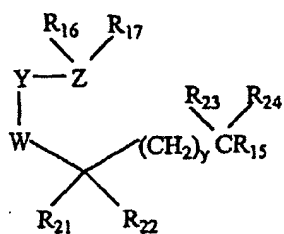
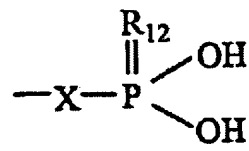


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Group VIII: Claims 1-23 (in part), drawn to products of the formula, wherein R_{23} and R_{24} are each H; R_{15}

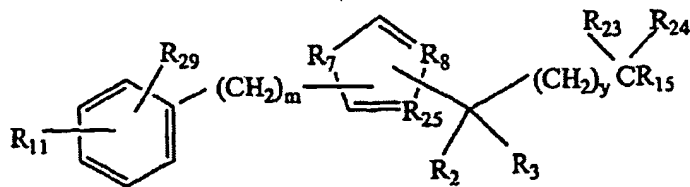
is $\text{—X—P} \begin{array}{l} \text{R}_{12} \\ \parallel \\ \text{OH} \end{array}$; R_{12} is O; X is O; y is 0; R_2 is NH_2 ; R_3 is H; R_7 is N; R_8 is S; R_{25} is CHR_{26} ; R_{26} is H; m is 0; R_{29} is H or halogen; and R_{11} is $\text{C}_5\text{—C}_{12}$ alkyl.

Group IX: Claim 24, drawn to a method for modulating the activity of an S1P receptor, comprising the step of contacting a compound of the formula

, wherein R_{23} and R_{24} are each H; R_{15} is

O; X is O; y is 0; R_{21} is NH_2 ; R_{22} is H; W is $(\text{CH}_2)_n\text{NH}(\text{CO})$; n is 0; Y is a bond; Z is CH_2 ; R_{16} is $\text{C}_5\text{—C}_{12}$ alkyl; and R_{17} is H.

Group IX: Claim 24, drawn to a method for modulating the activity of an S1P receptor, comprising the step of contacting a compound of the formula

, wherein R_{23} and R_{24} are each H; R_{15}

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$$\text{—X—P} \begin{array}{l} \text{R}_{12} \\ \parallel \\ \text{OH} \\ \text{OH} \end{array}$$
 is R_{12} is O; X is O; y is 0; R_2 is NH_2 ; R_3 is H; R_7 is N; R_8 is S; R_{25} is CHR_{26} ; R_{26} is H; m is 0; R_{29} is H or halogen; and R_{11} is $\text{C}_5\text{--C}_{12}$ alkyl.

Group X: Claims 25-27, drawn to a method of providing immuno-modulation to a patient in need thereof comprising administering a compound of the formula

$$\begin{array}{c} \text{R}_{16} \quad \text{R}_{17} \\ \diagdown \quad \diagup \\ \text{Y} \text{—} \text{Z} \\ | \\ \text{W} \text{—} \text{C} \begin{array}{l} \diagup \text{—} (\text{CH}_2)_y \text{—} \text{C} \begin{array}{l} \diagup \text{R}_{23} \quad \text{R}_{24} \\ \diagdown \text{R}_{15} \end{array} \\ \diagdown \text{R}_{21} \quad \text{R}_{22} \end{array} \end{array}$$
 , wherein R_{23} and R_{24} are each H; R_{15} is hydroxyl; y is 0; R_{21} is NH_2 ; R_{22} is H; W is $(\text{CH}_2)_n\text{NH}(\text{CO})$; n is 0; Y is a bond; Z is CH_2 ; R_{16} is $\text{C}_5\text{--C}_{12}$ alkyl; and R_{17} is H.

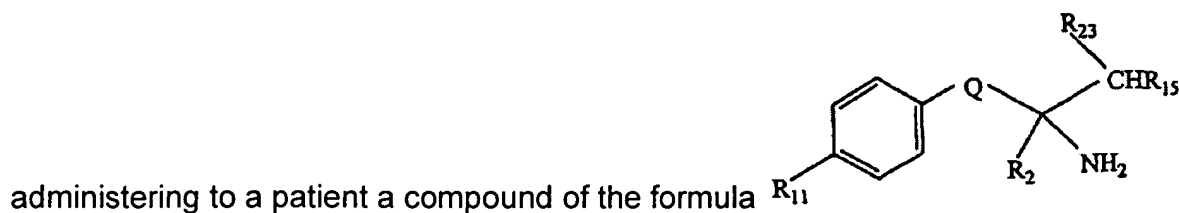
Group XI: Claims 25-27, drawn to a method of providing immuno-modulation to a patient in need thereof comprising administering a compound of the formula

$$\begin{array}{c} \text{R}_{16} \quad \text{R}_{17} \\ \diagdown \quad \diagup \\ \text{Y} \text{—} \text{Z} \\ | \\ \text{W} \text{—} \text{C} \begin{array}{l} \diagup \text{—} (\text{CH}_2)_y \text{—} \text{C} \begin{array}{l} \diagup \text{R}_{23} \quad \text{R}_{24} \\ \diagdown \text{R}_{15} \end{array} \\ \diagdown \text{R}_{21} \quad \text{R}_{22} \end{array} \end{array}$$

$$\text{—X—P} \begin{array}{l} \text{R}_{12} \\ \parallel \\ \text{OH} \\ \text{OH} \end{array}$$
 , wherein R_{23} and R_{24} are each H; R_{15} is O; X is O; y is 0; R_{21} is NH_2 ; R_{22} is H; W is $(\text{CH}_2)_n\text{NH}(\text{CO})$; n is 0; Y is a bond; Z is aryl; R_{16} is $\text{C}_5\text{--C}_{12}$ alkyl; and R_{17} is H.

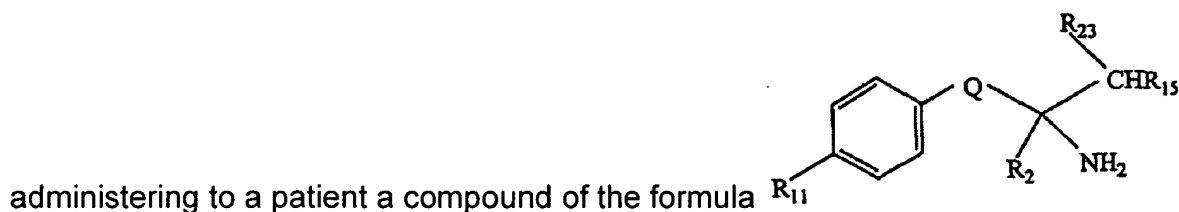
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Group XII: Claims 28-31, drawn to a method of treatment comprising



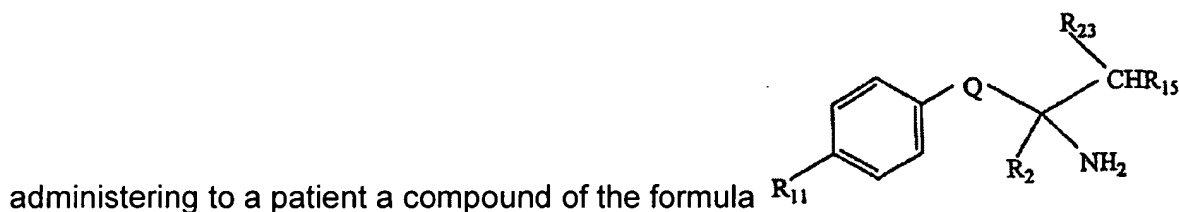
wherein Q is 1,3-thiazole.

Group XIII: Claims 28-31, drawn to a method of treatment comprising



wherein Q is triazole.

Group XIV: Claims 28-31, drawn to a method of treatment comprising



wherein Q is imidazole.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted. As stated above, this is not an exhaustive list, as it would be impossible to produce such a list under the time constraints due to the large volume of subject matter claimed in this application.

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The claims herein lack unity of invention under PCT Rules 13.1 and 13.2 because, pursuant to 37 C.F.R. 1.475(a) **Groups I-XIV** lack unity of invention since under 37 CFR 1.475:

Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical feature among those inventions involving one or more of the same or corresponding special technical features...those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

There is no structural moiety common to **Groups I-XIV** and no technical feature. Moreover, there is no "special" technical feature among claims 1-31. Therefore, claims 1-31 are not so linked as to form a single general inventive concept and there is a lack of unity of invention. The variables vary extensively and when taken as a whole result in vastly different compounds. Additionally, the vastness of the claimed subject matter and the complications in understanding the claimed subject matter impose a serious burden on any examination of the claimed subject matter.

Because the claims do not relate to a single general inventive concept under PCT Rule 13.1 and lack the same or corresponding special technical features, the claims lack unity of invention and should be limited to a product, a process for the manufacture of said product, or a method of use.

Furthermore, with respect to **Groups I-XIV**, even if unity of invention under 37 CFR 1.475(a) is not lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

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- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specially designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specially designed for carrying out the said process.

Moreover, according to 37 CFR 1.475(c),

If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

In the instant case the claims are drawn to more than one product, process, and method of use. According to 37 CFR 1.475(e),

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

As a result, the claims lack unity of invention and applicant is required to elect a single invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even if the restriction requirement is traversed (37 CFR 1.143).

Telephone Inquiry

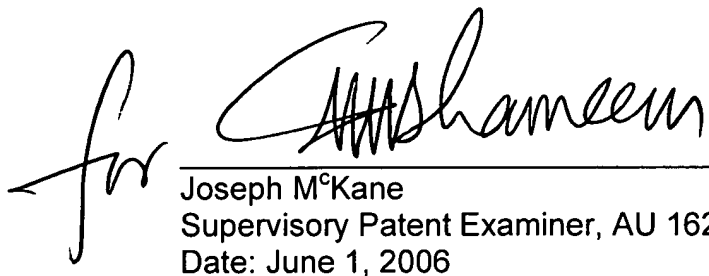
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached on 8:30 am - 5:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^cKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Andrew B. Freistein
Patent Examiner, AU 1626

The signature is handwritten in black ink. It consists of a large, stylized 'J' followed by 'M Kane'. The signature is written over a horizontal line.

Joseph M^cKane
Supervisory Patent Examiner, AU 1626
Date: June 1, 2006